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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,233	02/28/2002	Maria Alexandra Glucksmann	MPI01-021P1RNM	6932

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MILLENNIUM PHARMACEUTICALS, INC.
40 Landsdowne Street
CAMBRIDGE, MA 02139

EXAMINER	
BASI, NIRMAL SINGH	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/085,233	GLUCKSMANN, MARIA ALEXANDRA	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29 and 32-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29 and 32-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/23/05,4/18/03*, 7/9/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed 6/23/05 has been entered.

2. IDS file 7/9/02, 4/8/03 and 6/23/05 have been considered.

Election/Restriction

3. Applicant's election of Group VI, Claims 28 and 29 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)). Applicant has cancelled claims 1-27, 30-31 and added new claims 32-43. Claims 28-29 and 32-43 will be examined. The requirement is still deemed proper and is therefore made FINAL.

4. **Objections**

The disclosure is objected to because of the following informalities:
The specification contains numerous incomplete sentences, which contain lines instead of words, e.g. page 5, paragraph 0023. The lines appear inappropriately in the sentences.
Appropriate correction is required throughout the specification.

The specification should be reviewed for improper recitation of hyperlinks. All such recitations should be deleted or amended such that the hyperlinks are rendered inactive. See MPEP 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 29, 32, 37-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite because it is not clear what is "direct detecting" of binding so as to allow the metes and bounds of the claim to be determined. Further it is not clear if "test compound/polypeptide binding" refers to test compound binding to polypeptide or something else. It is suggested to overcome the rejection the "direct binding" be clarified and "test compound/polypeptide binding" amended to test compound binding to the polypeptide.

Claim 32 is indefinite because it is not clear what is "directly and indirectly labeled" so as to allow the metes and bounds of the claim to be determined. For example what is "indirect labeling".

Claim 29 is indefinite because it is not clear what is "93870-mediated signal transduction" and how the detection of binding of a test compound to the polypeptide is determined by "an assay for 93870-mediated signal transduction". What aspect of the assay for 93870-mediated signal transduction shows that the test compound has bound to the polypeptide.

Claims 40, 41 are also rejected for use of "93870-mediated signal transduction" for the reasons given above

Claim 41 is indefinite because it is not clear what "mobilization of a molecule" and what aspect of said mobilization shows that the test compound has bound to the polypeptide.

Claims 37-39 and 42 are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC 101 and 35 USC 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 28-29 and 32-43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A specific utility is a utility that is specific to the subject matter claimed, as opposed to a general utility that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specifications disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A well established utility must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 28-29 and 32-43. Claims are drawn to method of identifying compounds that bind to 93870 polypeptide having the amino acid sequence disclosed in SEQ ID NO:2, which is encoded by nucleic acid sequence disclosed in SEQ ID NO: and SEQ ID NO:3. 93870 polypeptide is disclosed to have structural characteristics in common with members of the G protein-coupled receptor family. 93870 is expressed in a variety of tissues (see page 94 for example).

The **specification does not disclose** the following as they pertain to the GPCR of SEQ ID NO:2:

a) significant structural homology of the GPCR of SEQ ID NO:2 to any known GPCR, which could be used to predict functional activity or its signal transduction pathway.

b) the individual regions of the GPCR of SEQ ID NO:2 that form the seven transmembrane regions,

c) the catalytic domain of the GPCR of SEQ ID NO:2

d) the specific G protein that couples to the GPCR of SEQ ID NO:2 (different g proteins interact with different GPCRs and have different physiological effects)

e) the natural ligand that binds the GPCR of SEQ ID NO:2

f) specific diseases that are directly related to said GPCR dysfunction

g) the activity regulated by the GPCR of SEQ ID NO:2

h) diseases that can be treated by the candidate compound identified by binding to the GPCR of SEQ ID NO:2

i) experimental data on the functionality of the GPCR of SEQ ID NO:2

j) the specific activity of claimed GPCR

k) no ligands that bind or activate the GPCR are disclosed

Applicant has classified the GPCR of SEQ ID NO:2 into the superfamily of GPCRs. The specification discloses the GPCR of SEQ ID NO:2 can be used to identify test compounds which bind said receptor. The GPCR of SEQ ID NO:2 is disclosed is to be potentially involved in a variety of unrelated disease states. It noted that neither the specific activity of GPCR of SEQ ID NO:2 or the specific treatable disease associated with the GPCR of SEQ ID NO:2 is disclosed. There is no disclosure of the specific activity of claimed GPCR. There is no disclosure of how to specifically use the compound identified by claimed method. Further no ligands that bind or activate said GPCR are disclosed. In light of the

specification the skilled artisan cannot come to any conclusions as to the function of the 93870 polypeptide G protein-coupled receptor of SEQ ID NO:2. The utility of claimed 93870 polypeptide cannot be implicated solely from homology to the proteins known in the art because the art does not provide teaching stating that all protein disclosed have the same activity, same effects, the same ligands and are involved in the same disease states (discussed later). In light of the specification and art the skilled artisan cannot come to any conclusions as to the function of protein of instant invention. There is no disclosure provided within the instant specification on what specific function the protein of SEQ ID NO:2 possesses, or how to use compounds that bind said protein. No disease states are disclosed that are directly related to 93870 polypeptide dysfunction.

The specification fails to disclose, what disease is associated with claimed receptor dysfunction or what drugs effect a specific claimed receptor function. The GPCR may have utility in the future, when it has been further characterized (e.g. its dysfunction or function correlated with a disease state) and its ligand characterized. The inclusion in the family of G protein coupled receptors (GPCR) does not constitute either a specific and substantial asserted utility or a well established utility for that particular GPCR or protein. This is analogous to all proteins or GPCRs can be used as protein markers on a gel.

Specification discloses claimed receptors are useful in screening but the specification does not disclose what claimed receptor specifically regulates and what specific disease the receptor is a target for. What would be the use of using the claimed receptor on a panel for drug screening? The receptor has no known

ligand or known function. How would one use the compounds that interacted with said orphan receptors? The specification provides a diverse list of disease states that may be involved in receptor dysfunction. It is unpredictable what ligands will bind to orphan receptors, and further the functional effects of ligand binding may remain uncertain even after extensive experimentation. What is the utility for a ligand, in many cases with no known function, that binds to a receptor of no known function? The ordinary artisan can only speculate on the utility for the ligand and receptor. A utility to orphan receptor cannot be assigned without knowledge of what disease is associated with claimed receptor dysfunction or what drugs/ligands effect a specific claimed receptor function. The superfamily of G-protein-coupled receptors are highly divergent in their effects and include receptors for hormones, neurotransmitters, paracrine substances, inflammatory mediators, certain proteinases, taste and odorant molecules, and even photons and calcium ions. Members of a sub-family of G-protein-coupled receptors are also highly divergent in their effects, as highlighted by Murdoch et al (Blood, Volume 95, No.10, pages 3032-3043, 2000), in the discussion of cytokine G-protein-coupled receptors. The utility of claimed receptor cannot be implicated solely from homology to known G-protein coupled receptors or their protein domains because the art does not provide teaching stating that all members of family of G-protein coupled receptors must have the same effects, the same ligands and be involved in the same disease states, the art discloses evidence to the contrary. The specification has not even used protein domains/homology to predict the activity of the protein. Murdoch discloses the

superfamily of G-protein-coupled receptors are highly divergent in their effects and include receptors for hormones, neurotransmitters, paracrine substances, inflammatory mediators, certain proteinases, taste and odorant molecules, and even photons and calcium ions. Members of a sub-family of G-protein-coupled receptors are also highly divergent in their effects, as highlighted by Murdoch et al, in the discussion of cytokine G-protein-coupled receptors. Further, the G-protein that interacts with the claimed orphan receptor and is required for the signal transduction activity is unknown. Watson (The G-Protein Linked receptor Facts Book, pages 2-6 and 223-230, 1994) states "it has therefore not been possible to identify consensus amino acid sequences that confer G-protein specificity, and thus G-protein interactions cannot be predicted from the primary amino acid sequence". Therefore the disclosure of Watson predicts, using the primary structure of the G-protein coupled receptor the skilled artisan cannot predict its associated G-protein or its ligand. G-protein coupled receptors are highly specialized and ligand specific proteins. The superfamily of seven transmembrane domain G-protein coupled receptors are specialized proteins designed for chemical recognition of ligands and subsequent transduction of information encoded in those ligands to the machinery of the cell, and the G-protein coupled receptors interact with alkaloids, biogenic amines, peptides, glycoprotein hormones, light and odorents (Terry Kenakin, Pharmacological Reviews, Vol. 48, No.3, pages 413-462), see page 413. Kenakin also states, "To achieve information transfer, the ability to bind ligands to a recognition domain and allosterically transmit the presence of that ligand to an intracellular domain

appears to be a specialized feature of 7TM receptors. The very properties that define receptors as such also impart unique protein behaviors to receptors, and these behaviors, in turn, affect drug activity", page 414, column 1, second paragraph. Bork (Nature Genetics, Vol 18, pages 313-318, 1998) provide a review article disclosing the problems of using homology detection methods to assigning function to related members of a family. Bork discloses: a) "While current homology detection methods can cope with data flow, the identification, verification and annotation of functional features need to be drastically improved", page 313, column 1, Abstract, b) there are two bottle necks that need to be overcome en route to efficient functional predictions from protein sequences, i.e., "First, there is the lack of a widely accepted, robust and continuously updated suite of sequence analysis methods integrated into coherent and efficient prediction system. Second, there is considerable 'noise' in the presentation of experimental information, leading to insufficient or erroneous function assignment in sequence databases", page 313, column 1, third paragraph, c) "In-depth analysis of protein sequences often results in functional predictions not attained in the original studies", page 313, column 2, last paragraph, d) "However, more often than not, it is clear that the cellular role of the protein in question differs from that of the detected homologue(s) and there is currently no automatic means to establish how much functional information can be legitimately transferred by analogy from homologue to the query", page 315, column 2, last paragraph, e) pertaining to predictions of protein function, "Do not simply transfer functional information from the best hit. The best hit is frequently

hypothetical or poorly annotated; other hits with similar or even lower scores may be more informative; even the best hit may have a different function", while "many proteins are multi functional; assignment of a single function, which is still common in genome projects, results in loss of information and outright errors" and "It is typical that the general function of a protein can be identified easily but the prediction of substrate specificity is unwarranted; for example, many permeases of different specificity show approximately the same level of similarity to each other", page 316. Karp (Bioinformatics, Vol 14, No.9, pages 753-754, 1998) has disclosed the problems of using functional prediction based on homology analysis. Karp states, a) "Although we know the accuracy with which sequence homologs can be determined, we know little about the accuracy of the overall process of assigning function by homology, page 753, column 2, second paragraph, b) "We have more faith in the correctness of those sequences whose functions we determined experimentally, rather than through computational means, page 753, column 2, last paragraph, c) "research is required to estimate the error rate of functional annotation by different methods of computational sequence analysis", page 754, column 2, last paragraph. Bork (Current Opinion in Structural Biology, Vol 8, pages 331-332, 1998), discusses the problems with deriving biological knowledge from genomic sequences and states, "structural similarity does not lead to iron-clad functional predictions" page 331, column 2 last paragraph, "Structural similarity does not necessarily mean a common evolutionary origin" page 332, column 1, second paragraph, and "Today, what we predict from sequences is at best fragmentary and qualitative", page 332,

column 2, second paragraph. Therefore, references discussed above disclose the unpredictability of assigning a function to a particular protein based on homology, especially one that belongs to the family of GPCRs, which have very different ligand specificity and functions.

It can be argued the GPCR of SEQ ID NO:2 is useful tool as a reagent or a molecular target in the diagnosis and treatment of GPCR mediated disorders. All members of the GPCR protein family have a utility in selectively screening of candidate drugs that target GPCRs. However, for a utility to be well-established it must be specific, substantial and credible. In this case, as all receptors are in some combination useful in selectively screening of candidate drugs that target GPCRs and in toxicology testing. However, the particulars of screening of candidate drugs, that target GPCR of SEQ ID NO:2, and in toxicology testing are not disclosed in the instant specification. Neither the candidate drugs or toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility, which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to GPCR of SEQ ID NO:2. Because of this, such a utility is not specific and does not constitute a well-established utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed protein for screening compounds that are a target for GPCR of SEQ ID NO:2 is only useful in the sense that the information that is gained from the assay and is dependent on the effect it has on the protein, and says nothing

with regard to each individual member of the GPCR family. Again, this is a utility, which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants individual GPCR is affected by a test compound in an assay for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed method of using claimed GPCR has no well-established use. The artisan is required to perform further experimentation on the claimed GPCR itself in order to determine to what use any information regarding this protein could be put.

With regard to diagnosis of disease, in order for a protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the GPCR of SEQ ID NO:2 and a disease or disorder. The presence of GPCR of SEQ ID NO:2 in tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed GPCR and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the GPCR of SEQ ID NO:2 to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the GPCR of SEQ ID NO:2 is either present only in, e.g. cancer tissue to the exclusion of normal tissue or is expressed in higher levels in

diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of the GPCR of SEQ ID NO:2 as a diagnostic for a disease. However, in the absence of any disclosed relationship between the GPCR of SEQ ID NO:2 and any disease or disorder and the lack of any correlation between the claimed GPCR with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing. *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

Further, GPCR of SEQ ID NO:2 belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family. The diversity of the GPCRs has already been described. Without some common biological activity for the family members, a new member would not

have a specific or substantial utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities, which may be related to tissue distribution, but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for drug screening, toxicology testing and diagnosis, is to argue a general, nonspecific utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed GPCR, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible real world manner based on the diversity of biological activities possessed by the GPCR family. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient

likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The assertion that the claimed invention has utility in drug screening, drug development and disease diagnosis, do not meet the standards for a specific, substantial or well-established utility for reasons set forth above. None of the utilities identified have been demonstrated to be specific to the polypeptide of SEQ ID NO:2 . One of ordinary skill in the art must understand how to achieve an immediate and practical benefit from the claimed species based on the knowledge of the class. However, no practical benefit has been shown for the use of the polypeptide SEQ ID NO:2. Applicant has failed with respect to GPCR of SEQ ID NO:2, has not described the family of GPCRs in enough detail to show, by a preponderance of the evidence, that the polypeptide of SEQ ID NO:2 has any substantial use. The record shows that the family of proteins having GPCR domains is diverse, and has such a broad definition, that a common utility cannot be defined. Moreover, the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner,* the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for

possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention.

The use of the claimed invention for toxicology testing, drug discovery, and disease diagnosis are not substantial utilities. The question at issue is whether or not the broad general assertion that the GPCR of SEQ ID NO:2 might be used for some diagnostic application in the absence of a disclosure of which diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.)

The prior rejection under 101 followed *Brenner v. Manson*. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was

not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. A rejection under 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967). Further since the claimed GPCR has no utility, methods of its use are also rejected for lack of utility.

7. Claims 28-29 and 32-43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a real world context of use for the method of identifying compounds that bind theGPCR of SEQ ID NO:2, further experimentation is necessary to attribute a utility to the GPCR of SEQ ID NO:2 and methods of using said receptor in screening agents as possible therapeutics. The claims fail to disclose how to use the claimed invention for the reasons given above (lack of utility). Further the claims are drawn to an orphan GPCR whose activity, associated G-protein and activating ligands have not been disclosed.

Neither the claims nor the specification disclose what specific biological activity is associated with the GPCR of SEQ ID NO:2. There is no disclosure of the specific compounds that are activated in the signal transduction pathway or what ligand is capable of binding to the GPCR of SEQ ID NO:2, so as to disclose a specific function for said GPCR. There is no disclosure of how to assay activity since the natural ligand and function of GPCR of SEQ ID NO:2 is unknown.

The complex nature of GPCRs and the unpredictability of assigning a function to a receptor with no known ligand or function is described in the rejection under 35 USC 101 and 35 USC 112, 1st paragraph, see the teachings of Murdoch, Watson, Kenakin, Karp and Bork, disclosed above.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. Further for an agent to be a candidate therapeutic agent, the dysfunction associated with the GPCR of SEQ ID NO:2 must be known. In instant case it is not known what dysfunction is associated with the GPCR of SEQ ID NO:2. The question is even if a an agent does bind to with the GPCR of SEQ ID NO:2 or regulates its expression, then what? Applicant still has to find a therapeutic use of said agent. The activity regulated by the GPCR of SEQ ID NO:2 is unknown.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on 571272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nirmal S. Basi
Art Unit 1646
September 19, 2005

JOSEPH MURPHY
PATENT EXAMINER